

wherein a positively-charged amino acid residue in the hairpin loop structure of wild-type HGF has been replaced with an amino acid residue with no charge or a negative charge for use in medicine.

33. (new) A variant human hepatocyte growth factor (HGF) according to Claim 31 wherein at least amino acid residue R73 has been replaced by an amino acid residue with no charge or with a negative charge for use in medicine.

34. (new) A variant human hepatocyte growth factor (HGF) according to Claim 31 wherein at least amino acid residue R76 has been replaced by an amino acid residue with no charge or with a negative charge for use in medicine.

35. (new) A variant human hepatocyte growth factor (HGF) according to Claim 31 wherein both amino acid residues R73 and R76 have been replaced independently with an amino acid residue with no charge or with a negative charge for use in medicine.

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Cont. 36. (new) A variant hepatocyte growth factor (HGF) according to Claim 31 which is a human HGF comprising amino acid residue replacements R73E and R76E for use in medicine.

37. (new) A variant hepatocyte growth factor (HGF) according to Claim 31 which is a human HGF comprising amino acid residue replacements R73E, R76E and R93E for use in medicine.

38. (new) A variant hepatocyte growth factor (HGF) according to Claim 31 which is a human HGF comprising amino acid residue replacements R73E, R76E and K78E for use in medicine.

39. (new) A variant hepatocyte growth factor (HGF) according to Claim 31 which is a human HGF consisting of human HGF with amino acid replacements R73E and R76E for use in medicine.

40. (new) A variant hepatocyte growth factor (HGF) according to Claim 31 which is a human HGF consisting of human HGF with amino acid replacements R73E, R76E and R93E for use in medicine.

41. (new) A variant hepatocyte growth factor (HGF) according to Claim 31 which is a human HGF consisting of human HGF with amino acid replacements R73E, R76E and K78E for use in medicine.

42. (new) A variant hepatocyte growth factor (HGF) according to Claim 31 which antagonises the action of wild-type HGF for use in medicine.

43. (new) A variant hepatocyte growth factor (HGF) according to Claim 42 wherein the variant HGF further comprises a mutation which confers resistance in the variant HGF to proteolytic cleavage by enzymes capable of *in vivo* conversion of HGF into its two-chain form for use in medicine.

44. (new) A variant human hepatocyte growth factor (HGF) according to Claim 43 which have an amino acid alteration at or adjacent to any of amino acids 493, 494, 495 and 496 of the wild-type human HGF.

45. (new) A pharmaceutical composition comprising a variant hepatocyte growth factor (HGF) as defined in Claim 31 and a pharmaceutically acceptable carrier.

46. (new) A method of treating a patient in need of treatment with a hepatocyte growth factor or an antagonist thereof the method comprising administering to the

patient an effective amount of a variant HGF as defined in Claim 31.

47. (new) A method according to Claim 46 wherein the patient has cancer.

48. (new) A method of manufacturing a medicament comprising admixing a variant hepatocyte growth factor (HGF) as defined in Claim 31 and a carrier.

49. (new) A variant hepatocyte growth factor (HGF) which is substantially incapable of binding heparan sulphate proteoglycan but which is capable of binding to the HGF receptor provided that the variant HGF is not a variant of human HGF in which the replacements (a) R73E, R76E and R93E or (b) R73E and R76E or (c) K91E, R93E and K94E have been made.

50. (new) A variant hepatocyte growth factor (HGF) according to Claim 49 wherein a positively-charged amino acid residue in the hairpin loop structure of wild-type HGF has been replaced with an amino acid residue with no charge or with a negative charge.

51. (new) A variant human hepatocyte growth factor (HGF) according to Claim 49 wherein at least amino acid residue R73 has been replaced by an amino acid residue with no charge or with a negative charge.

52. (new) A variant human hepatocyte growth factor (HGF) according to Claim 51 wherein at least amino acid residue R76 has been replaced by an amino acid residue with no charge or with a negative charge.

53. (new) A variant human hepatocyte growth factor (HGF) according to Claim 49 wherein both amino acid residues R73 and R76 have been replaced independently with an amino acid residue with no charge or with a negative charge.

54. (new) A variant human hepatocyte growth factor (HGF) comprising amino acid residue replacements R73E and R76E; or amino acid residue replacements R73E, R76E and R93E; or amino acid residue replacements R73E, R76E and K78E; or amino acid replacements R73E and R76E; or amino acid replacements R73E, R76E and R93E.

55. (new) A variant hepatocyte growth factor (HGF) according to Claim 49 which antagonises the action of wild-type HGF.

56. (new) A variant hepatocyte growth factor (HGF) according to Claim 55 wherein the variant HGF further comprises a mutation which confers resistance in the variant HGF to proteolytic cleavage by enzymes capable of *in vivo* conversion of HGF into its two chain form.

57. (new) A variant human hepatocyte growth factor (HGF) according to Claim 56 which have an amino acid alteration at or adjacent to any of amino acids 493, 494, 495 and 496 of the wild-type human HGF.

58. (new) A polynucleotide encoding a variant hepatocyte growth factor according to Claim 31.

59. (new) A vector comprising a polynucleotide according to Claim 58.

60. (new) A host cell comprising a polynucleotide according to Claim 58.

61. (new) A host cell comprising a vector according to Claim 59.

62. (new) A method of producing a variant hepatocyte growth factor (HGF) the method comprising culturing a cell as defined in Claim 60 and isolating the variant HGF therefrom.